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Null Results in Brief

Cancer Epidemiology, Biomarkers & Prevention

No Association between Radiation Dose from Pediatric CT Scans and Risk of Subsequent Hodgkin Lymphoma

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Abstract

Background: We examined the relationship between estimated radiation dose from CT scans and subsequent Hodgkin lymphoma in the UK pediatric CT scans cohort.

Methods: A retrospective, record linkage cohort included patients ages 0 to 21 years who underwent CT scans between 1980 and 2002 and were followed up for cancer or death until 2008. Poisson regression analysis was used to evaluate the relationship between estimated radiation dose (lagged by 2 years) and incident Hodgkin lymphoma diagnosed at least 2 years after the first CT scan.

Results: There were 65 incident cases of Hodgkin lymphoma in the cohort of 178,601 patients. Neither estimated red bone marrow dose nor mean lymphocyte dose from CT scans was clearly associated with an increased risk of Hodgkin lymphoma (RR for 20+ mGy vs. <5 mGy = 0.92 (0.38–2.22) $P_{trend} > 0.5$ and 1.44 (0.60–3.48) $P_{trend} > 0.5$), respectively.

Conclusions: Radiation exposure from pediatric CT scans 2 or more years before diagnosis was not associated with Hodgkin lymphoma in this large UK cohort.

Impact: These findings are consistent with the majority of previous studies, which do not support a link between ionizing radiation and Hodgkin lymphoma. The results contrast our previous positive findings in this cohort for brain tumors and leukemia, both of which are known to be strongly linked to radiation exposure during childhood. *Cancer Epidemiol Biomarkers Prev; 26(5); 804–6. ©2017 AACR.*

Introduction

Hodgkin lymphoma is one of the few cancers not associated with ionizing radiation exposure (1). It was unexpected, therefore, that a recent study reported an increased risk of Hodgkin lymphoma among those who ever had a pediatric CT scan at least a year before their cancer diagnosis (2). That finding was interpreted by some as evidence that studies of pediatric CT scans and cancer risk are biased due to reverse causation (3). In a recent publication on potential biases, including cancer predisposing conditions and reverse causation, we noted that these biases will vary by cancer type, analytic methods, calendar period, and study location and should not be generalized (4).

Here, we report results from the UK pediatric CT scan study, where we examined the relationship between radiation dose from CT scans and subsequent risk of Hodgkin lymphoma in a cohort of approximately 180,000 children. To minimize potential biases, we evaluated a dose response rather than ever/never exposed, excluded patients diagnosed with Hodgkin lymphoma within 2 years after their first CT scan to reduce the impact of reverse causation as CT is commonly used to diagnose Hodgkin lymphoma, and evaluated the effect of excluding patients with predisposing conditions.

Materials and Methods

This is a retrospective, record linkage cohort study with an internal comparison group. The study methods were described previously (5). Briefly, radiology databases from 81 National Health Service regions in the United Kingdom were searched for CT scans performed for ages 0 to 21 years between 1980 and 2002. These records were linked to the National Health Service Central Register for outcome information, including cancer registrations, deaths, and emigration. Patients with a cancer diagnosis prior to or within the first 2 years following the date of their first recorded CT were excluded.

Radiation dose was estimated for each CT according to age, calendar year, sex, and body region scanned. As the location of cells that ultimately develop into Hodgkin lymphoma is uncertain, we estimated red bone marrow (RBM; ref. 6), as used in most previous studies, and mean lymphocyte doses. Mean lymphocyte dose was estimated as a weighted average of dose to the lymph nodes, RBM, blood, spleen, thymus, and small intestine with weights determined by the proportion of lymphocytes in each tissue (7).

For the current analysis, the outcome was a first cancer diagnosis of Hodgkin lymphoma. We assessed associations between radiation dose (lagged by 2 years for the primary analysis or 5 years for a sensitivity analysis) and Hodgkin lymphoma with Poisson linear RR models adjusting for attained age. To avoid

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inclusion of CT scans related to cancer diagnosis, we began accrual of person-time 2 years after the first CT and continued accrual until the date of first cancer diagnosis or the earliest of death, loss to follow-up, or December 31, 2008. We reviewed available clinical information for unreported previous cancers and underlying conditions that could be related to Hodgkin lymphoma, including immune-related conditions (8) and Rothmund–Thomson syndrome (9).

Results

In the cohort of 178,601 eligible patients, 65 Hodgkin lymphoma cases were diagnosed during follow-up at a mean age of 21 years (range, 2–33 years). Mean RBM dose was 12 mGy overall (range = 0–689 mGy) and 11 mGy in the cases (range = 0–133 mGy), and mean lymphocyte dose was 8 mGy (range = 0–348 mGy) overall and 9 mGy (range = 1–65 mGy) in the cases. Neither estimated RBM nor mean lymphocyte dose from CT scans was associated with an increased risk of Hodgkin lymphoma [RR for 20+ mGy vs. <5 mGy = 0.92; 95% confidence interval (CI), 0.38–2.22; $P_{trend} > 0.5$ and 1.44; 95% CI, 0.60–3.48; $P_{trend} > 0.5$; Fig. 1]. Sensitivity analysis with dose lagged by 5 rather than 2 years yielded similar results (RR for 20+ mGy vs. <5 mGy = 0.60; 95% CI, 0.21–1.69; $P_{trend} > 0.5$ for RBM and 0.80; 95% CI, 0.25–2.58; $P_{trend} = 0.35$ for mean lymphocyte dose; Fig. 2). Exclusion of four cases with underlying Hodgkin lymphoma–related conditions (2× transplants, Rothmund–Thomson syndrome, immunocompromised) and a possible misdiagnosed non-Hodgkin lymphoma did not alter the findings (data not shown).

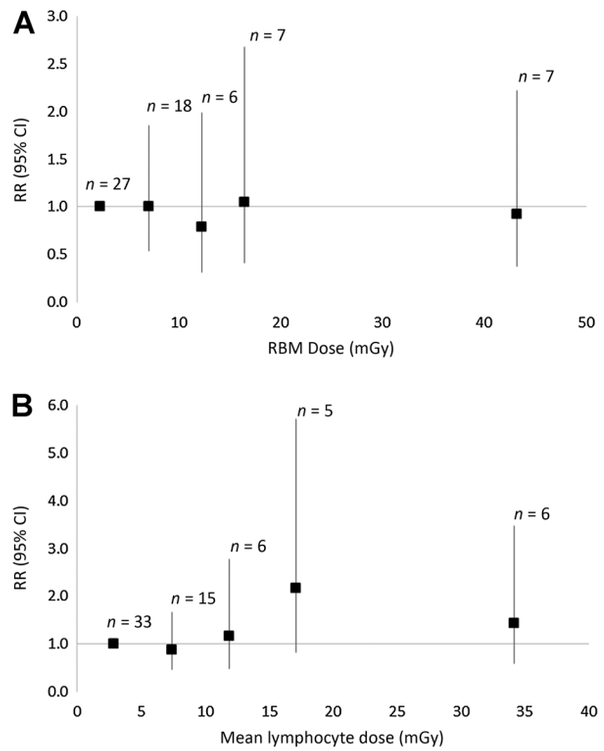

Figure 1.
RR for Hodgkin lymphoma in relation to estimated radiation dose from pediatric CT scans: 2-year dose lag. **A,** RBM dose. P_{trend} (categorical) > 0.5 and excess RR/mGy = 0.002 (−0.016 to 0.021). *n* = number of cases in each dose category. **B**, Mean lymphocyte dose*. P_{trend} (categorical) > 0.5 and excess RR/mGy = 0.028 (−0.024 to 0.080). *n* = number of cases in each dose category. *Age-specific weighted average of organ doses to the RBM, spleen, lymph nodes, thymus and small intestine, blood, and outside hematopoietic tissues (7).

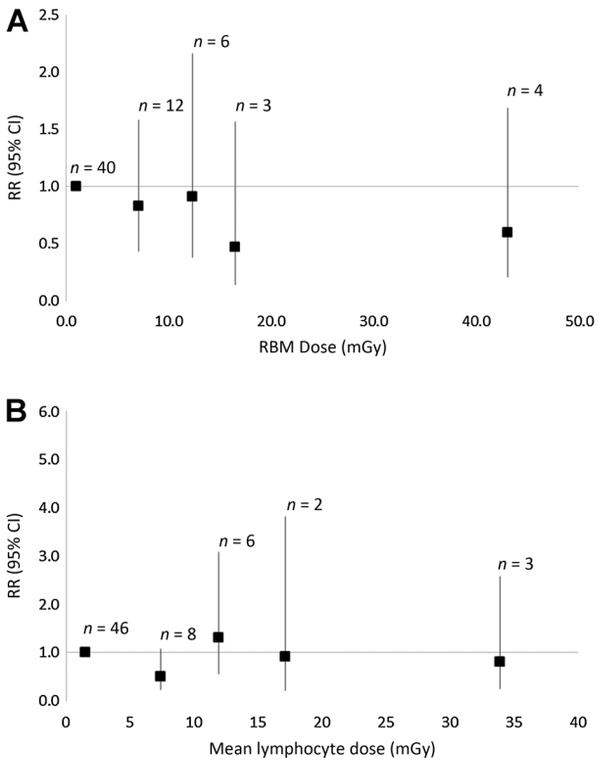

Figure 2.
RR for Hodgkin lymphoma in relation to estimated radiation dose from pediatric CT scans: 5-year dose lag. **A,** RBM dose. P_{trend} (categorical) > 0.5 and excess RR/mGy = −0.001 (−0.016 to 0.013). *n* = number of cases in each dose category. **B,** Mean lymphocyte dose*. P_{trend} (categorical) = 0.35 and excess RR/mGy = −0.003 (−0.027 to 0.022). *n* = number of cases in each dose category. *Age-specific weighted average of organ doses to the RBM, spleen, lymph nodes, thymus and small intestine, blood, and outside hematopoietic tissues (7).

Discussion

We found no evidence of a relationship between radiation exposure from pediatric CT scans and Hodgkin lymphoma in our large retrospective cohort. This is consistent with most previous studies of ionizing radiation, including the Life Span Study of atomic bomb survivors, nuclear workers, and patients who underwent radiotherapy (1), and in contrast with the Australian pediatric CT study (2). Differences between the analytic approaches could explain this discrepancy. We excluded cancers diagnosed within 2 years of the first reported CT scan (including 257 cases of HL), rather than one year, to reduce reverse causation and evaluated a dose response rather than ever-never exposed. The most relevant organ dose for Hodgkin lymphoma is uncertain, but circulating lymphocytes are likely to be critical, and our novel estimate of mean lymphocyte dose was designed to capture this. We will continue to follow up this cohort, but the current analysis does not provide evidence of a relationship between radiation dose from pediatric CT scans and subsequent risk of HL. These

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results provide an important contrast with our findings in this cohort for brain tumors and leukemia (5), which are known to be strongly linked to radiation exposure (1).

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Authors' Contributions

Conception and design: A. Berrington de Gonzalez, L. Parker
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Acquisition of data (provided animals, acquired and managed patients, provided facilities, etc.): A. Berrington de Gonzalez, R.W. Harbron, A.W. Craft, M.S. Pearce
Analysis and interpretation of data (e.g., statistical analysis, biostatistics, computational analysis): A. Berrington de Gonzalez, N. Journy, C. Lee, L.M. Morton, D.R. Stewart, L. Parker, A.W. Craft, K. McHugh, M.P. Little, M.S. Pearce
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Administrative, technical, or material support (i.e., reporting or organizing data, constructing databases): R.W. Harbron, A.W. Craft
Study supervision: L. Parker
Other (clinical and radiology input): K. McHugh

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